

**REMARKS/ARGUMENTS**

**Status of the Claims**

Upon entry of the present amendment, claims 18-23, 32, 34-35 and 37-43 are pending. Claims 18-23, 32, 34-35, 37-39 are amended, and new claims 40-43 are added.

Claim 18 is amended to set forth a solution comprising a pair of FRET hybridization probes. Support is found, for example, on page 3, lines 5-23 and on page 8, lines 12-15.

Claim 19 is amended for proper antecedent basis to depend from claim 18.

Claim 20 is amended to set forth a solution and to remove "a" preceding 3 oligonucleotides. Support is found, for example, on page 8, lines 12-15.

Claims 21-23 are amended for proper antecedent basis to depend from claims 18 and 20.

Claim 32 is amended to set forth a solution comprising a pair of FRET hybridization probes. Support is found, for example, on page 3, lines 5-23 and on page 8, lines 12-15.

Claim 34 is amended for proper antecedent basis to depend from claim 32.

Claim 35 is amended to set forth a solution and to remove "a" preceding "3 oligonucleotides." Support is found, for example, on page 8, lines 12-15.

Claim 37 is amended for proper antecedent basis to depend from claim 35 and to insert "the" preceding "FRET donor entity."

Claims 38 and 39 are amended for proper antecedent basis to depend from claims 32 and 35. Claim 39 is amended to insert a comma between "a nucleic acid amplification primer" and "a template dependent nucleic acid polymerase."

New claims 40-42 set forth a solid support and track the language of claims 18, 20 and 32, respectively. Support is found, for example, on page 3, lines 5-23 and on page 8, lines 12-15.

New claim 43 sets forth a kit comprising the solution of any one of claims 18, 20, 32 and 35.

New claim 44 sets forth a kit in the language of previously presented claim 35, found allowable by the Examiner.

New claim 45-49 set forth that the solutions are lyophilized. Support is found, for example, on page 11, lines 19-20.

No new matter is added by the above amendments.

**Telephone Interview**

Applicants thank the Examiner for graciously granting the telephonic interview of May 24, 2006. The issues discussed are set forth in the presently pending Official Action. Agreement was reached regarding claim language that would overcome the cited art, as discussed below.

**Claim Objections**

**Claim 35**

The Examiner objected to claim 35, requesting the removal of the article "a" preceding "3 oligonucleotides." In response, Applicants have amended claim 35 to remove the article "a" preceding "3 oligonucleotides."

**Claim 39**

The Examiner objected to claim 39, requesting that a comma be inserted between "a nucleic acid amplification primer" and "a template dependent nucleic acid polymerase." In response, Applicants have inserted a comma between "a nucleic acid amplification primer" and "a template dependent nucleic acid polymerase."

**Rejection under 35 U.S.C. 102(b) over U.S. Patent No. 5,866,336 (Nazarenko)**

The Examiner rejected claim 22 under 35 U.S.C. § 102(b) as allegedly anticipated by Nazarenko. To the extent that this rejection applies to amended claim 22, this rejection is respectfully traversed.

“A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). M.P.E.P. § 2131.

Applicants respectfully disagree with the Examiner regarding the alleged anticipation of claim 22 by Nazarenko. However, in the interest of furthering prosecution, Applicants have amended claim 22 to set forth a solution depending from, and therefore containing all of the elements of, claims 18 and 20. Amended claims 18 and 20 are directed to solutions comprising two oligonucleotides that are a FRET pair: the first carries a FRET donor of the FRET pair and a quenching moiety; the second carries a FRET acceptor of the FRET pair. Nazarenko does not disclose or suggest a solution comprising two oligonucleotides that are a FRET pair as set forth in the claims. Instead, Nazarenko discloses using the upstream hairpin primer comprising FAM and a quencher in one experiment (disclosed at column 38 and Figure 24 A-G), and using the reverse primer labeled with rhodamine in another experiment (disclosed at column 35 and Figure 13A).

Since Nazarenko does not disclose or suggest the claimed solutions, Nazarenko does not anticipate the claims. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

**Rejection under 35 U.S.C. 102(e) over U.S. Patent No. 6,579,680 (Frutos patent)**

The Examiner has rejected claims 22 and 38 under 35 U.S.C. § 102(e) as allegedly anticipated by the Frutos patent. Applicants respectfully disagree with the Examiner. However, in the interest of prosecution, Applicants have amended claims 22 and 38 to set forth a solution, and depend from claims 18 and 20 or 32 and 35, respectively.

Claim 18 and 32 set forth that the FRET donor entity of the first oligonucleotide and the FRET acceptor entity of the second oligonucleotide are a **FRET pair**. Claims 20 and 35 set forth that the first oligonucleotide and the third oligonucleotide are each labeled with one corresponding member of a **FRET pair** consisting of a FRET donor entity and a FRET acceptor entity. In each of claims 18, 20, 32 and 35 the oligonucleotide carrying the FRET donor entity of the FRET pair further carries an entity capable of quenching fluorescence of the FRET donor entity.

The Frutos patent does not disclose or suggest a FRET pair donor and a quencher of the FRET pair donor on one oligonucleotide and a FRET pair acceptor on another oligonucleotide, as recited in the amended claims. At most, Frutos discloses an oligonucleotide comprising two different acceptor moieties (*e.g.*, DABCYL and 5-nitroindole). Frutos specifically and repeatedly teaches that the 5-nitroindole moiety is incorporated into the quencher probe (*see, e.g.*, column 3, lines 55-61 and column 7, lines 24-29). Moreover, the Examiner in attempting to construct this anticipation rejection, the Examiner has alluded to other fluorescent moieties not disclosed in the Frutos patent (*e.g.*, a green fluorescent protein), and therefore not a member of any FRET pair in Frutos.

Because the Frutos patent does not disclose or suggest the claimed solutions, the Examiner is respectfully requested to withdraw this rejection.

**Rejection under 35 U.S.C. 102(a) over Frutos, JACS (2002) 124:2396 (Frutos manuscript)**

The Examiner has rejected claims 22 and 38 under 35 U.S.C. § 102(a) as allegedly anticipated by the Frutos manuscript. This rejection is respectfully traversed for the same reasons discussed above for the Frutos patent. The Frutos manuscript does not disclose or suggest a FRET pair donor and a quencher of the FRET pair donor on one oligonucleotide and a FRET pair acceptor on another oligonucleotide. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

**Rejection under 35 U.S.C. 103(a) over Nazarenko in view of Stratagene catalog**

The Examiner has rejected claims 18-21 and 23 under 35 U.S.C. § 103(a) as allegedly rendered obvious by Nazarenko in view of the 1988 Stratagene catalog.

Applicants respectfully disagree with the Examiner. However, in the interest of furthering prosecution, Applicants have amended the rejected claims to set forth solutions comprising the first, second and third oligonucleotides of the inventions, clarifying that at least two of the oligonucleotides are a FRET pair. As discussed above, Nazarenko does not disclose or suggest using the primers identified by the Examiner in a solution. Furthermore, the Stratagene catalog, which is cited for its disclosure of a kit, does not cure the defects of Nazareko.

Because the combined disclosures of Nazarenko and the Stratagene catalog do not disclose or suggest the claimed solutions, the Examiner is respectfully requested to withdraw this rejection.

**Rejection under 35 U.S.C. 103(a) over Frutos manuscript in view of Stratagene catalog**

The Examiner has rejected claims 18, 19, 32, 34 and 39 under 35 U.S.C. § 103(a) as allegedly rendered obvious by the Frutos manuscript in view of the 1988 Stratagene catalog.

Applicants respectfully disagree with the Examiner. However, in the interest of furthering prosecution, Applicants have amended the rejected claims to set forth solutions comprising the oligonucleotides of the inventions, clarifying that the oligonucleotides are a FRET pair. As discussed above, neither the Frutos patent nor the Frutos manuscript discloses or suggests an oligonucleotide carrying a FRET pair donor moiety and a moiety capable of quenching the donor moiety. Furthermore, the Stratagene catalog, which is cited for its disclosure of a kit, does not cure the defects of Frutos.

Because the combined disclosures of Frutos and the Stratagene catalog do not disclose or suggest the claimed solutions, the Examiner is respectfully requested to withdraw this rejection.

Appl. No. 10/621,428  
Amdt. dated June 7, 2006  
Reply to Office Action of February 13, 2006

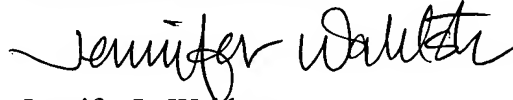
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**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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